

Gaze-dependent phoria and vergence adaptation

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Incomitance is a condition with gaze-dependent deviations of ocular alignment and is common in strabismus patients. The physiological mechanisms that maintain equal horizontal ocular alignment in all gaze directions (concomitance) in healthy individuals are poorly explored. We investigate adaptive processes in the vergence system that are induced by horizontal incomitant vergence stimuli (stimuli that require a gaze-dependent vergence response in order to re-establish binocular single vision). We measured horizontal vergence responses elicited after healthy subjects shifted their gaze from a position that required no vergence to a position that required convergence. Repetitive saccades into a position with a convergence stimulus rapidly decreased phoria (defined as the deviation of ocular alignment in the absence of a binocular stimulus). This change of phoria was present in all viewing directions (from 0° to $0.86^\circ \pm 0.40^\circ$, $p < 0.001$) but was more pronounced in the gaze direction with a convergence stimulus (from $0.26^\circ \pm 0.13^\circ$ to $1.39^\circ \pm 0.33^\circ$, $p < 0.001$). We also found that vergence velocity rapidly increased ($p = 0.015$) and vergence latency promptly decreased ($p < 0.001$). We found gaze-dependent modulation of phoria in combined saccade–vergence eye movements and also in pursuit–vergence eye movements. Thus, acute horizontal, gaze-dependent changes of vergence, such as may be encountered in new onset strabismus due to paralysis, can rapidly increase vergence velocity and decrease latency. Gaze-specific (concomitant) and gaze-independent (incomitant) phoria levels will adapt. These early adaptive processes increase the efficacy of binocular vision and maintain good ocular alignment in all directions of gaze.

Introduction

Strabismus is a misalignment of the visual axes and can be classified into a manifest (tropia) and a latent (phoria) deviation of the eyes. Tropia is characterized by ocular misalignment despite binocular stimulation. Phoria appears only in monocular condition when binocular stimulation is absent (Kaufmann, 2004; Leigh & Zee, 2006). Orthotropia is achieved when the visual axes of the eyes converge on a binocular target. It is a prerequisite for binocular vision and stereopsis. Orthophoria is achieved if ocular alignment is maintained even in the absence of binocular stimulation (Maddox, 1907). If ocular alignment fails, strabismus results. Strabismus is termed concomitant if the angle of deviation is constant in all directions of gaze. In incomitant strabismus, the angle varies with the direction of gaze (Michaelides & Moore, 2004). If ocular alignment is artificially disrupted (for example, if a prism is placed in front of one eye) the result is binocular disparity, which triggers a vergence eye movement to re-establish ocular alignment (Dysli, Keller, & Abegg, 2015). If the disparity is too large to be fused, double vision results. Whereas horizontal disparities are easier to fuse, vertical disparities soon lead to double vision. If a prism is worn for a long time, phoria equal in power and opposite in direction to the prism will be evident at the end of the adaptation period. This phenomenon is called prism adaptation or phoria adaptation (Maxwell & Schor, 1994; C. M. Schor, 1983; Sethi & North, 1987). Phoria adaptation is an adaptation of the tonic vergence component. This serves to re-establish a new equilibrium as starting position for further vergence eye movements and thus decreases the effort for either convergence or divergence eye movements. If the artificially inserted prism is removed, phoria gradually

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reverts to the value it had before the prism was placed (Milder & Reinecke, 1983). By this mechanism, the vergence system is fine-tuned continuously so that the eyes maintain alignment. Prism adaptation has been mostly investigated in primary gaze. But ocular alignment is important in all viewing directions. Like prism adaptation in primary gaze, there may be adaptive mechanisms that correct for incomitant misalignment and cause concomitant orthophoria (ocular alignment in all directions of gaze). There are several lines of evidence that suggest such a mechanism exists:

- Over 100 years ago, Bielschowsky (1907) made the clinical observation that an incomitant strabismus becomes increasingly concomitant over time, also called “spread of comitance” (von Noorden & Campos, 2002) or “orthophorization” (Kaufmann, 2004; Leigh & Zee, 2006). Its underlying mechanisms are not yet understood.
- Afocal magnifying lenses that induced vertical incomitant disparity provided evidence of the mechanism (Graf, Maxwell, & Schor, 2003; Henson & Dharamshi, 1982; Maxwell & Schor, 1994). The phoria response this stimulus produced was maximal at the eye position at which the adaptation stimulus was presented. In the past, an incomitant phoria adaptation has been demonstrated for *vertical* incomitance (for a review, see Maxwell & Schor, 2006). No study has investigated *horizontal* incomitant vergence or adaptation to horizontal incomitance in humans. In monkeys however, Oohira and Zee (1992) have measured horizontal phoria.
- Prolonged occlusion of one eye in healthy, non-strabismic individuals leads to incomitant vertical phoria with elevation of the adducting eye (Graf, Maxwell, & Schor, 2002; Liesch & Simonsz, 1993). This experiment shows that when the continuous fine-tuning of ocular alignment is disrupted, nonstrabismic subjects develop incomitant strabismus.

To understand the physiological mechanisms that support comitance, we investigated adaptive processes to a new onset, horizontal, gaze-dependent binocular disparity. We thus tested two hypotheses. First, we tested whether horizontal incomitant disparity caused incomitant phoria adaptation (a gaze-dependent decrease of phoria in the gaze direction with the largest disparity). To determine how specific and robust the incomitant vergence adaptation was, we tested our first hypothesis in two separate experiments: a saccade–vergence eye movement paradigm and a pursuit–vergence eye movement paradigm. Second, we tested in the saccade–vergence paradigm whether vergence response velocity and latency improved as it had in our previous study (Dysli et al., 2015).

Materials and methods

Subjects

In the first experiment, there were 11 healthy, nonstrabismic subjects (six female, five male; median age 27 years; range 16 to 49 years). Five subjects were emmetropic, five subjects had mild or moderate myopia (<4 diopters [dpt]), and one subject was presbyopic. In the second experiment, there were 12 nonstrabismic subjects (six female, six male; median age 26 years; range 16 to 49 years). Seven of these also participated in the first experiment. Six subjects were emmetropic, five subjects had mild myopia (<2 dpt), and one subject was presbyopic. Exclusion criteria were strabismus, double vision, and large refractive error.

Ethical approval

The local ethics committee (Bern, Switzerland) approved of the study, and all subjects gave informed written consent in accordance with the Declaration of Helsinki.

Apparatus

We used an infrared video-based eye tracker to record movements of both eyes at 1000 Hz (EyeLink 1000 V 4.56, SR Research Ltd., Mississauga, ON, Canada). The experiment was programmed in Experiment Builder software (SR Research). To present stimuli independently to each eye, we used a haploscopic setup that consisted of two thin film transistor liquid crystal displays (TFT-LCD, 22-in., 75 Hz, 1024 × 768 pixels, LG, South Korea) located on each side of the subject and two mirrors at 45° placed in front of the subject. This setup led to the impression of one screen located straight ahead of the subject. The optical distance from the forehead to the screen was 54 cm. Head position was stabilized with a chin and a forehead rest.

The optical system was aligned at the beginning of the experiment. We aligned central stimuli on the left- and right-side screens by shifting the screens until the subject saw the stimulus as a single image. We moved the screens laterally, so viewing distance remained unchanged. Then we used the alternate cover test to fine-tune the screens until no phoria was detectable when we switched fixation from the left stimulus viewed with the left eye to the right stimulus viewed with the right eye. Nine reference points, presented only to the left eye, were used to calibrate the eye tracker binocularly for each subject. This canceled out any

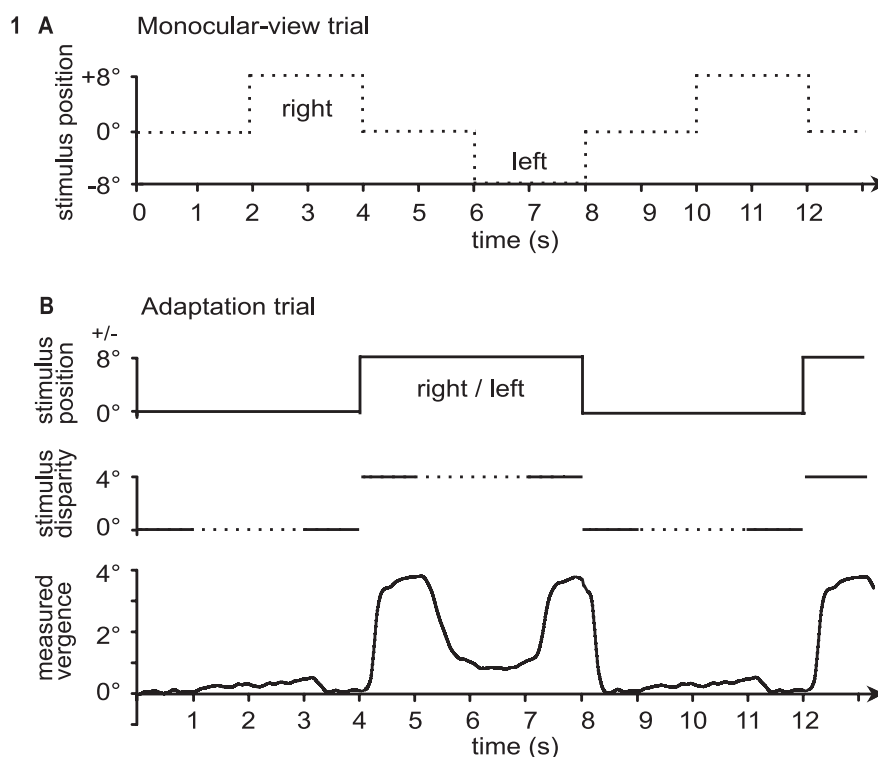


Figure 1. Experimental design of Experiment 1. (A) In monocular-view trials, stimuli were visible to only one eye. Stimuli started in the subject's midsagittal plane and changed horizontal position every 2 s to 8° on the right, back to the center, and to 8° on the left. (B) Adaptation trials started with binocular fixation stimulus. After an interval of 1 s, the stimulus of one screen was extinguished for 2 s (monocular view, dashed line) and then reappeared for 1 s. The midsagittal stimulus was then replaced by a stimulus located 8° to one side with a horizontal disparity of 4°, which required a convergent eye movement for fusion (bottom). Lateral stimuli were also binocularly visible for 1 s, followed by monocular view for 2 s and binocular view for 1 s. No disparity was present for the midsagittal stimulus.

preexisting phoria or incomitance, normalizing possible phoria to zero (resulting in orthophoria in all gaze directions). Calibration was accepted if accuracy was below 1°.

Stimuli

Experiment 1

The first experiment consisted of three monocular-view blocks (10 trials each) and two adaptation blocks (80 trials each) (Figure 1A, B). The monocular-view blocks assessed the level of phoria in three gaze positions: before the first adaptation, after adaptation to one gaze direction, and after adaptation to a second gaze direction. The stimulus was a black cross in the center of a circle (diameter 2°) on a white background. In a monocular-view block trial, the stimulus shifted in position from the subject's midsagittal plane 8° to the right, back to the midsagittal plane, and then 8° to the left. The stimulus changed position every 2 s and was visible only to the right eye.

Each trial in the adaptation block began with a binocular fixation stimulus in the subject's midsagittal plane. After 1 s, the stimulus on the left screen was extinguished for 2 s (monocular view, dotted line in Figure 1B) and then reappeared for 1 s. Then a stimulus located 8° to one side replaced the midsagittal stimulus and remained binocularly visible for 1 s. This was followed by monocular view for 2 s. The trial ended with a 1-s binocular view. Subjects were told to visually track the stimuli. The stimuli on the side were presented with a horizontal crossed disparity of 4°, which required a moderate convergent eye movement for fusion. Shifting the stimulus on one of the monitors resulted in binocular disparity. Subjects thus performed asymmetrical vergence steps into the right or left visual field, but there was no disparity for the midsagittal stimulus (no symmetrical vergence step). For half of the subjects, in the first adaptation, block side stimulus was 8° on the right for 80 consecutive trials, and in the second adaptation, side stimulus was 8° on the left, also for 80 trials. For the other half of the subjects, we reversed the order of direction (the

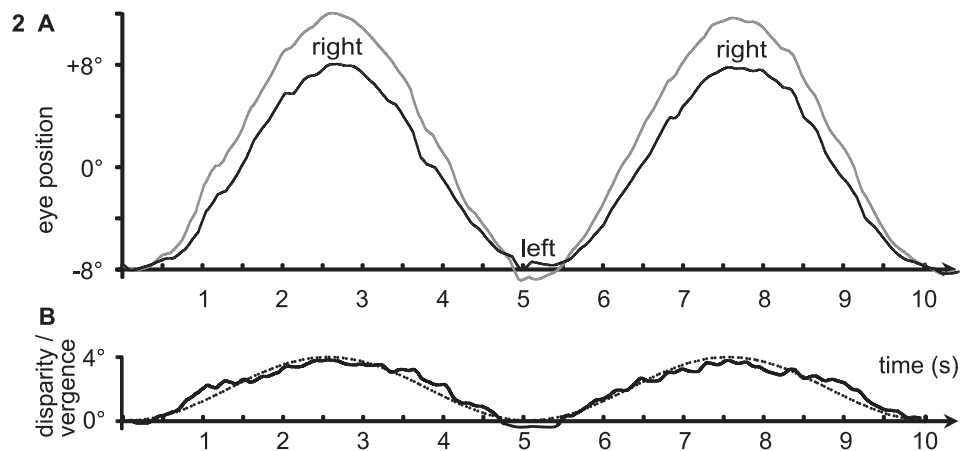


Figure 2. Experimental design of Experiment 2. (A) Sinusoidal vergence movements were elicited with stimuli that moved from 8° on the left to 8° on the right with increasing image disparity in the right gaze (black = right eye; gray = left eye). Recording of eye movements of one subject. (B) Disparity of stimuli (dashed curve) and measured vergence (solid curve) during the sinusoidal movement in (A).

first adaptation used left-side disparity, and the second adaptation used right-side disparity).

Experiment 2

To find out if the spatial dependency of phoria adaptation is limited to saccadic eye movements, we changed the viewing position with smooth pursuit eye movements instead of saccades. As in Experiment 1, we used two monocular-view blocks (10 trials each) located before and after an adaptation block (160 trials). Subjects were shown sinusoidal horizontally moving stimuli with a velocity of 6.4°/s (0.2 c/s, 1 cycle = 1 trial) and an excursion of 16°. The trials always started with the stimulus 8° on the left. The stimulus moved to 8° on the right and back to the left again. During the monocular-view blocks, the stimulus was presented only to the left eye, but during the adaptation block, the stimulus was presented binocularly (on both screens); it started in orthophoric position on the left with increasing disparity toward the right side. Image disparity was highest on the rightmost point, where the image disparity was 4° (Figure 2). During the adaptation block, the stimulus was presented monocularly in one out of five trials.

Data analysis

Vergence was determined by subtracting the horizontal gaze position of the left eye from that of the right eye. Positive values represent convergent eye position; negative values represent divergent eye position. We used the SR Research EyeLink Data Viewer V 1.11.1, Excel (Microsoft), and Clampfit V 10.3.1.4 (2011, Molecular Devices, LLC) to analyze the

data. Trials with incomplete data or trials in which subjects blinked were excluded from further analysis. We thus excluded 20% of the trials in Experiment 1 and 6% of the trials in Experiment 2.

Experiment 1

We normalized vergence by subtracting the mean vergence value of the monocular-view block, measured in the subject's midsagittal plane (0–2000 ms), from all vergence values. Vergence in primary gaze is thus zero, by definition. To measure the level of phoria during the adaptation blocks, we calculated the difference of mean amplitude from 950–1000 ms to 2950–3000 ms after stimulus onset (see Figure 3A). Trials with missing or incomplete values within this time span were excluded.

To assess the level of phoria in fully monocular conditions (before the vergence response had decayed), we measured the level of phoria by conducting monocular-view trials in three gaze directions (midsagittal plane, right, left) before and after the subject had adapted to one gaze direction and after the subject had adapted to a second gaze direction. We used mean amplitudes of the whole 2-s span of one gaze direction.

To measure the kinetics of the vergence response, we determined mean velocity by calculating the mean slope for the interval 10% to 90% of the vergence response. We used the time span from the onset of the vergence stimulus to the peak velocity of the vergence response as a measure of vergence latency (Figure 3A) (Dysli et al., 2015).

Statistical analysis

For statistical analysis, we used linear mixed effects models. Mean phoria level, mean vergence

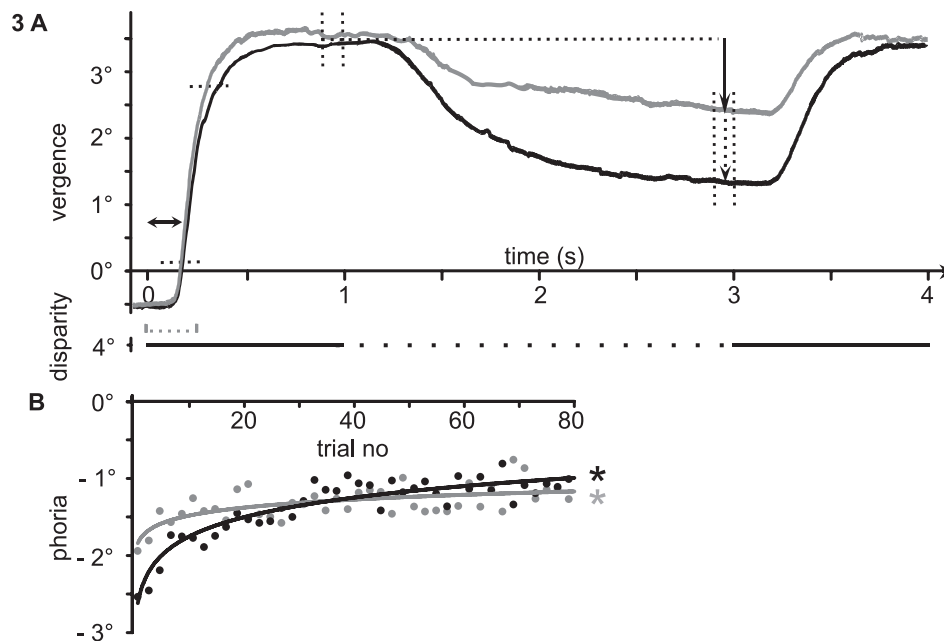


Figure 3. Incomitant phoria adaptation. (A) Averaged vergence responses from the first 10 (black) and the last 10 (gray) consecutive vergence eye movements of all subjects. Vergence stimulus (target disparity of 4°) was provided at 0 ms after a saccade into a field of gaze with increased disparity. After 1 s, the stimulus was viewed monocularly for 2 s, which caused vergence to decay. The stimulus was displayed binocularly again, 3 s after initial vergence stimulus. This provided a disparity of 4° and again elicited a vergence eye movement. We assessed phoria level (vertical arrows) by subtracting the mean amplitude between 950 and 1000 ms from the mean amplitude between 2950 and 3000 ms (vertical dashed lines). Vergence latency was defined as a period of time that began with onset of the vergence stimulus and ended when the curve reached peak velocity (horizontal arrow). Mean vergence velocity was determined for the length of time it took for the amplitude of the vergence curve to rise from 10% to 90% of its final value (short horizontal dashed lines). (B) Phoria adaptation over 80 trials for the first adapted direction (black) and for the second adapted (opposite) direction (gray). Phoria adapts significantly ($p < 0.001$) for both gaze directions. Adaptation to the second side is significantly different than it was for the first gaze direction ($p < 0.001$).

velocity, or mean vergence latency were dependent variables. Independent variables were direction of adaptation (first/second) and trial number. Trial number was the measure of time. We defined the change of a dependent variable over subsequent trials as “adaptation.” Subjects were used as a random effect. For the monocular-view trials, we used a mixed effects analysis to compare the change in phoria before and after first adaptation. Phoria level was the dependent variable, and order of direction of adaptation (first/second) was the independent variable. We investigated phoria differences in the three directions (midsagittal/right/left) for the time points “before first adaptation,” “after first adaptation,” and “after second adaptation.” The smaller-is-better principle, based on Akaike’s information criterion, governed our choice of fitting model (random-intercept, random-slope, or combined). We reported p values and 95% confidence intervals. Analyses were performed using the MIXED procedure in SPSS (IBM SPSS Statistics 21).

Experiment 2

To assess phoria, we analyzed the monocular-view trials before and after adaptation to a gaze-dependent image disparity. To achieve normalization, the mean of the left gaze (0–50 ms) of the monocular-view trials was subtracted from all vergence values. To investigate gaze-dependent phoria, we subtracted the mean phoria from the left gaze from the mean phoria of the right gaze (2450–2500 ms) before and after adaptation. To investigate gaze-independent (concomitant) adaptation, we compared the latter values before and after adaptation.

All trials with missing or incomplete values within these time spans were excluded. We again used linear mixed effects models: Mean phoria level was the dependent variable, direction (left/right) was the independent variable, and subjects were the random effect. Next we investigated every fifth trial from the adaptation block in which the stimulus had been presented monocularly. Here as well, the phoria of the

				95% confidence interval	
	Degrees of freedom	Significance (<i>p</i>)	Mean change per 10 trials	Lower bound	Upper bound
Phoria adaptation during experiment					
First direction	788.027	<0.001	−0.15	−0.02	−0.01
Second direction	788.038	<0.001	−0.05	−0.01	0.00
First versus second direction	1576.303	<0.001			
Monocular view after adaptation to first gaze direction					
Adapted first direction	30.793	0.001			
Midsagittal	30.964	0.006			
Nonadapted direction	31.623	0.005			
Monocular view after adaptation to second gaze direction					
Adapted second direction	22.959	0.802			
Midsagittal	21.600	0.974			
Nonadapted direction	22.452	0.396			
First versus second direction	301.952	0.006			

Table 1. Adaptation of phoria during experiment and during monocular view block.

left gaze was subtracted from the phoria of the right gaze. This difference (dependent variable) was tested for adaptation over time; trial number was the independent variable.

Results

Experiment 1

Changing the gaze from the subject's midsagittal plane without image disparity to a side view with an image disparity of 4° caused convergent eye movements. When the binocular stimulus was extinguished, vergence decayed in the first trials of the adaptation block (Figure 3A, black line). Over 80 consecutive trials, this decay of convergence gradually diminished. Phoria level gradually increased from $-2.85^\circ \pm 0.07^\circ$ (mean \pm SEM) to $-1.25^\circ \pm 0.09^\circ$ ($p < 0.001$, Table 1, Figure 3B). Switching from adaptation in one gaze direction to adapting vergence stimulus in the opposite direction again led to a significant adaptation of the phoria level after 80 trials (from $-2.00^\circ \pm 0.10^\circ$ to $-1.54^\circ \pm 0.09^\circ$, $p < 0.001$). Adaptation in the second gaze direction was significantly faster than in the first gaze direction ($p < 0.001$).

Next, we compared the level of phoria with monocular-view trials (no vergence stimulus in all gaze directions). This level was measured before adaptation, after adaptation to a first gaze direction, and after adaptation to a second gaze direction. Adaptation to a first gaze direction significantly increased phoria level in all gaze directions ($p = 0.001$ for the first adapted gaze direction, $p = 0.006$ for the midsagittal plane, $p =$

0.005 for the nonadapted direction, Figure 4). The increase of phoria was significantly larger in the adapted gaze direction (increase from $0.26^\circ \pm 0.13^\circ$ to $1.39^\circ \pm 0.33^\circ$) than in the midsagittal plane (from 0° to $0.87^\circ \pm 0.40^\circ$) or the gaze direction opposite the first adapted gaze direction (from $-0.02^\circ \pm 0.13^\circ$ to $0.84^\circ \pm 0.38^\circ$).

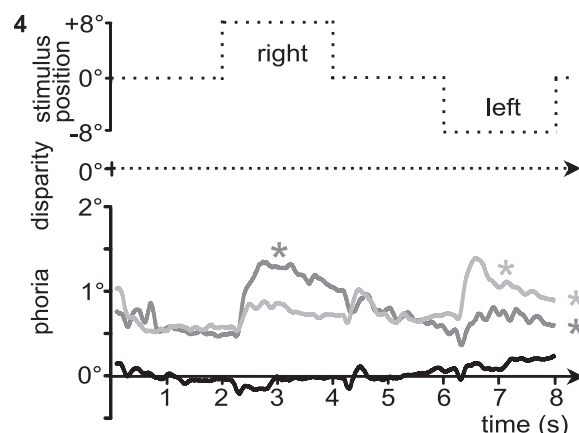


Figure 4. Incomitant and concomitant phoria adaptation. Averaged phoria of all subjects during monocular-view trials (no disparity). The asterisks on the right show gaze-independent phoria changes. Phoria levels are significantly different after adaptation to a disparity in right gaze (2–4 s, dark gray) and after adaptation in left gaze (6–8 s, bright gray) than they were before adaptation (black curve) (both p s < 0.001). Asterisks above the curve show gaze-dependent phoria changes with significant adaptation for the dark gray curve after adaptation to a disparity in right gaze ($p < 0.001$) and significant adaptation for the bright gray curve after adaptation in left gaze ($p = 0.006$).

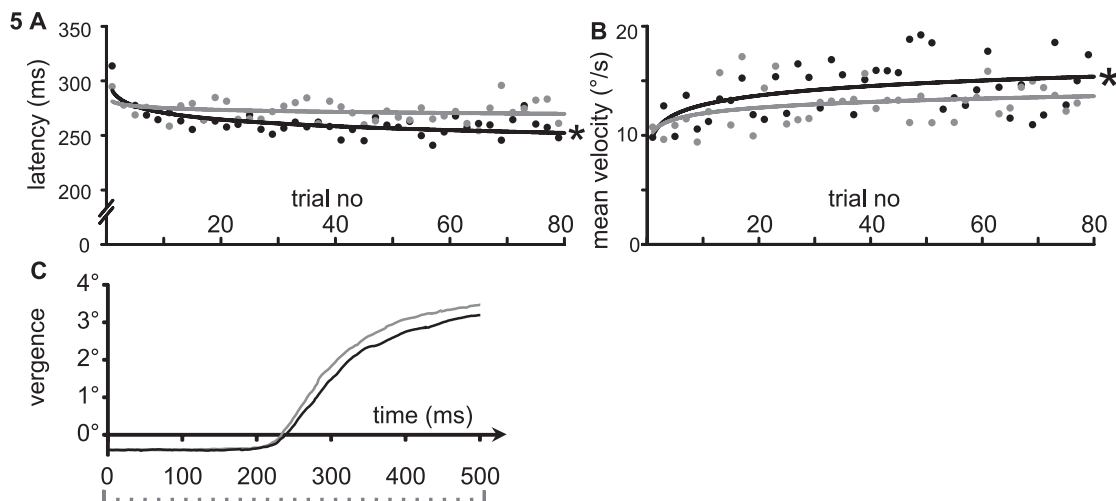


Figure 5. Adaptation of vergence kinetics and latency. Adaptation of vergence kinetics to the first lateral direction (black dots with black trend line) and the next second direction (gray dots with gray trend line). Asterisks indicate statistical significance. (A) Latency shows significant decrease during adaptation for the first disparity direction but no significant change during adaptation to the second direction. (B) Mean velocity for the first disparity direction shows significant increase. (C) Detailed view from the first 500 ms of the vergence curves shown in Figure 3A.

After adaptation to a second gaze direction, change of phoria was significantly different than it was for the first direction ($p = 0.006$). This indicates that phoria changed according to the direction of gaze. Adaptation to the second gaze direction left the phoria in the center unchanged ($0.87^\circ \pm 0.40^\circ$ after first adaptation, $0.86^\circ \pm 0.27^\circ$ after second adaptation, $p = 0.974$). Phoria level of the first adapted gaze direction, which had not been adapted during adaptation to a second gaze direction, slightly decreased (from $1.39^\circ \pm 0.33^\circ$ to $1.15^\circ \pm 0.22^\circ$, $p = 0.396$). In the second adapted gaze direction, phoria slightly increased (from $0.84^\circ \pm 0.38^\circ$ to $0.93^\circ \pm 0.26^\circ$, $p = 0.802$).

We then investigated the change of vergence velocity and latency over the course of 80 subsequent trials (Figure 5). During the first adaptation block, mean velocity of convergence response increased (from 9.82 to 15.00°/s, $p = 0.015$, Table 2) and latency decreased (from 313.71 to 257.27 ms, $p < 0.001$). During the second adaptation block, vergence kinetics did not

show significant adaptation (mean velocity changed from 10.75 to 12.96°/s, $p = 0.226$; latency changed from 294.65 to 283.31 ms, $p = 0.812$). Thus vergence kinetics (mean velocity and latency) adapted significantly to one gaze direction, but subsequent adaptation to a second direction of gaze did not reveal significant adaptation.

Experiment 2

In this experiment, we sought to determine if the directionally specific change of phoria level was limited to incommittance induced with saccades or if smooth pursuit eye movements would show comparable incommittant vergence adaptation. We thus compared the level of phoria from right gaze (first 50 ms) with left gaze (2450–2500 ms) from the monocular-view trials before and after the adaptation block. Before adaptation, phoria in left and right gaze was not significantly different ($p = 0.747$) (Table 3). After adaptation to

		95% confidence interval			
	Mean change per 10 trials	Lower bound	Upper bound	Degrees of freedom	Significance (<i>p</i>)
First adaptation					
Mean velocity (°/s)	−0.3	−0.06	−0.01	707.696	0.015
Latency (ms)	−2.24	−3.33	−1.15	707.142	<0.001
Second adaptation					
Mean velocity (°/s)	−0.2	−0.04	0.01	670.719	0.226
Latency (ms)	0.13	−0.91	1.16	667.310	0.812

Table 2. Adaptation of vergence kinetics.

	Mean change	95% confidence interval		Degrees of freedom	Significance (<i>p</i>)
		Lower bound	Upper bound		
Before adaptation (left vs. right)	0.17	−0.90	1.24	23.324	0.747
After adaptation (left vs. right)	−0.69	−0.98	−0.41	212.010	<0.001
Phoria in monocular-view block					
Nonadapted gaze direction	0.45	−0.67	1.57	23.837	0.417
Adapted gaze direction	1.27	−0.08	2.63	22.754	0.064
Monocular view during adaptation	0.05	−0.01	0.01	342.167	0.595

Table 3. Adaptation of incomitance induced with smooth pursuit (second experiment).

increased image disparity in right gaze, phoria in right gaze was significantly higher than phoria in left gaze ($p < 0.001$) (Figure 6). Next, we analyzed the vergence levels from the same gaze direction of the monocular-view blocks before and after the adaptation block. Adaptation in one gaze direction led to a nonsignificant gaze independent (concomitant) increase of phoria level in both the nonadapted (from $0^\circ \pm 0.49^\circ$ to $0.55^\circ \pm 0.64^\circ$, $p = 0.417$) and the adapted (from $-0.21^\circ \pm 0.66^\circ$ to $1.22^\circ \pm 0.79^\circ$, $p = 0.064$) gaze direction.

When we analyzed the monocular-view trials integrated in the adaptation block, we found no significant change of phoria over time ($p = 0.595$); no adaptation could be measured.

Discussion

Our experiments show that *horizontal* gaze-dependent vergence stimuli quickly induce a variety of changes: (a) We found global, gaze-independent (concomitant) adaptation of phoria (horizontal phoria was changed in left, midsagittal, and right horizontal planes). (b) We also found local, incomitant phoria adaptation (incomitant vergence stimuli rapidly induce phoria adaptation with the magnitude depending on gaze direction). (c) Analysis of phoria during incomitant adaptation trials revealed that adaptation occurs gradually over time, changing most within the first view trials. (d) Repetitive vergence eye movements become gradually faster and vergence latency shorter over time. These changes did not depend on gaze direction.

Concomitant phoria adaptation

After adaptation to an incomitant horizontal disparity, we found that phoria level was higher in all horizontal viewing directions and thus also in the gaze direction in which there had been no vergence stimulus (Figure 4). This resembles the well known “phoria adaptation” or “prism adaptation” described in several

studies (Kim, Vicci, Han, & Alvarez, 2011; Maxwell & Schor, 1994; C. M. Schor, 1983; Sethi & North, 1987). But majority of those studies investigated vertical phoria (Gleason, Schor, Lunn, & Maxwell, 1993; Graf et al., 2003; Maxwell & Schor, 1994; C. Schor, Gleason, Maxwell, & Lunn, 1993; C. M. Schor, Gleason, & Lunn, 1993) and not horizontal phoria (Henson & North, 1980; Oohira & Zee, 1992). In contrast to classical phoria adaptation, we did not expose our subjects to a continuous disparity stimulus. Instead, disparity changed based on time and gaze direction.

Incomitant phoria adaptation

In addition to the horizontal concomitant phoria adaptation, we found that phoria was significantly greater in the viewing direction in which the disparity was applied than in the nonadapted gaze direction. This incomitant phoria adaptation (first asterisk in Figure 4) is in some ways similar to the vertical incomitant phoria adaptation observed when subjects wore afocal magnifying lenses for a prolonged time. Those lenses create gaze-dependent image disparities with increasing disparity in vertical eccentric eye positions (Graf et al., 2003; Henson & Dharamshi, 1982; Maxwell & Schor, 1994).

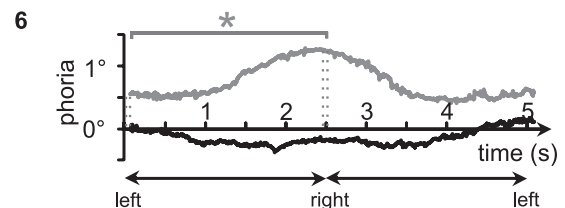


Figure 6. Incomitant phoria adaptation induced with smooth pursuit. Phoria from the monocular-view block performed before (black) and after (gray) adaptation to an image disparity of 4° in right gaze (at 2500 ms). Phoria level showed significant gaze-dependent change of phoria (asterisk) after adaptation. For statistical analysis, phoria was measured at time points indicated by vertical dashed lines.

Spread of adaptation

Change of phoria in nonadapted gaze directions has been described as “spread of adaptation” (C. Schor et al., 1993). The eye positions over which a locally applied change in vergence spreads is called the adaptive field. Oohira and Zee (1992) measured change of phoria across the visual field of monkeys when they coincidentally adapted to horizontal prisms of different magnitudes located in different positions. They found a gradual change instead of an abrupt change, which the prism combination required. Maxwell and Schor (1994) investigated the contrast between gradual and abrupt change of phoria across the visual field. They found that after a single disparity, adaptation spread in all gaze positions, but adaptation to opposite disparities in different locations resulted in position-specific adaptation of phoria. Our results are in line with a transfer of phoria adaptation to regions not exposed to image disparity. However, we tested horizontal phoria, and Maxwell and Schor (1994) tested vertical phoria. Although vergence adaptation is evident for both horizontal and vertical phoria, the horizontal vergence system is fundamentally different from the vertical vergence system. Vertical alignment does not change over time, but horizontal vergence depends on accommodation, the distance of objects, etc., and may thus be regulated independently or differently than vertical vergence. As a consequence, vertical amplitude of fusion is much smaller than horizontal amplitude (Sethi, 1986). From patients with abnormal binocular vision and deficient adaptation to horizontal prisms but normal vertical prism adaptation, we can assume that the two systems are regulated independently (North & Henson, 1981). Brautaset and Jennings (2005) confirmed this assumption by comparing horizontal and vertical prism adaptation in convergence insufficiency (CI) patients. They found that horizontal prism adaptation was reduced in CI patients but that vertical prism adaptation was the same as for controls. Stevenson, Lott, and Yang (1997) also postulated different controlling mechanisms for horizontal and vertical disparities. They found that horizontal vergence shows a strong voluntary component, but vertical vergence is almost exclusively reflexive.

Pursuit phoria adaptation

To explore whether the spatial dependency of horizontal phoria adaptation is linked to saccades only, we repeated the first experiment using smooth pursuit instead of saccades to change the viewing position. Here too, a gaze-independent and a gaze-dependent increase of phoria level could be observed. This raises the possibility that both saccades and pursuit adapta-

tion activate the same mechanisms. However, C. M. Schor, Gleason, and Horner (1990) found that vertical vergence accompanying pursuit can be adapted independently from vertical vergence accompanying saccades; i.e., adaptation of pursuit did not transfer to saccades and vice versa, which is inconsistent with our hypothesis. Because we did not measure monocular pursuit eye movements after adaptation to saccadic targets or phoria at saccadic targets after adaptation of sinusoidal smooth pursuit, our data are not suitable for testing this interdependency. Furthermore, Gleason et al. (1993) found that vertical vergence can be adapted with respect to pursuit in a direction-specific manner, which means that incomitant phoria adaptation is not simply tied to an eye position signal but perhaps a velocity or phase signal as well.

Time course of phoria adaptation

Our experimental design allowed us to determine the temporal dynamics of the adaptive response. We found an inverse exponential increase in phoria level during adaptation, starting within the first trials (Figure 3B). This gradual but rapid change illustrates that phoria increase is a true adaptive response. Brautaset and Jennings (2005) had similar results when they compared phoria adaptation in subjects with convergence insufficiency to age-matched controls. Henson and Dhar-amshi (1982) investigated the temporal course of adaptation of incomitant vertical phoria (i.e., more phoria in eccentric position of gaze) over more than 160 min and found that the incomitant level of phoria decreased during this time. Although the time constants acquiring concomitant (prisms) and incomitant (lenses) vertical phoria adaptation were similar, the time constants for the decay were quite different (Graf et al., 2003). Decay was significantly faster for prisms (concomitant), which suggests that different mechanisms are involved in concomitant and incomitant adaptation.

In contrast to the gradual adaptation of the phoria and vergence over time, saccadic disconjugacy (difference between saccadic amplitude of the left and the right eye) in combined saccade–vergence eye movements does not show adaptation: The change in saccadic disconjugacy is immediate and abrupt after subjects started to perform saccades to a more convergent stimulus (Eggert & Kapoula, 1995). The abrupt versus continuous change of the two kinds of eye movements suggests that different mechanisms contribute to saccadic disconjugacy and vergence adaptation (Averbuch-Heller, Lewis, & Zee, 1999; Gleason et al., 1993; C. M. Schor et al., 1993; C. M. Schor et al., 1990).

Adaptation to a second gaze direction, which followed adaptation of a first, opposite gaze direction, confirmed gaze-dependent and gaze-independent phoria adaptation (bright gray line in Figure 4). The temporal dynamics also showed incommittant and concomitant aspects (gray line in Figure 3B). Phoria already started at a higher phoria level. This can be explained by the concomitantly higher phoria level, which was adopted during adaptation to the first direction of gaze. Phoria adaptation from the second direction was significantly different than phoria adaptation of first adapted gaze direction.

Vergence dynamics

Finally, we analyzed the kinetics of horizontal vergence eye movements during adaptation (Figure 5). We found that the mean velocity increased within the first 20 trials and that the vergence latency decreased, confirming our earlier observations (Dysli et al., 2015). Few studies have investigated how disparity vergence or sustained fixation influences the dynamics of disparity vergence. Patel, Jiang, White, and Ogmen (1999) demonstrated that vergence dynamics depend on the initial vergence angle. Lee et al. (2009) and Satgunam, Gowrisankaran, and Fogt (2009) obtained the same results. Peak velocity decreased as the phoria became more esophoric and increased for exophoric shifts in the phoria. Ying and Zee (2006) did not study disparity vergence, but studied the decay of sustained fixation on a convergence stimulus of 30°. The dynamics of divergence decay were faster after short fixation than after long fixation. Kim, Granger-Donetti, Vicci, and Alvarez (2010) found baseline and adapted phoria correlating to convergence and divergence peak velocity asymmetries. They also showed that a subject's ability to adapt phoria significantly correlates to his or her ability to adapt dynamic disparity vergence peak velocity (Kim, Vicci, Granger-Donetti, & Alvarez, 2011). After sustained convergence, Satgunam et al. (2009) noted a convergent shift in phoria. Divergence latency increased whereas convergence latency (in contrast to our results) was unchanged. Recently, Lang et al. (2014) used gap and overlap tasks to investigate saccade–vergence properties over short-time repetition. In contrast to our findings in which latency quickly decreased within the first few trials, they could not find any change of latency over repetition in either of the two task conditions. Moreover, in the gap task, they showed mean and peak velocity decreased rather than the increase we measured. They defined the mean velocity as the ratio between amplitude and vergence duration, which might have biased their results. Phoria level

might decrease over time, and the vergence might not yet be completed after the recorded time span.

Takagi et al. (2001) found that vergence velocity increased after training with the double step paradigm, whereby the initial disparity changed just after vergence begins (adaptive recalibration).

In our study, we found that the vergence mean velocity of the second adapted direction no longer showed significant increase when compared to the first adapted direction. The missing increase could be explained by a possible transmission of the gained increase in vergence mean velocity by repetitive vergence eye movements into a preceding different viewing direction and would argue for a concomitant gain of vergence mean velocity, which is not direction-dependent.

If the findings of Patel et al. (1999) and Lee et al. (2009) are also applicable for convergence eye movements, change in phoria might explain the different dynamics here as well. However, the fact that it did not increase more could also be attributed to increasing fatigue. In the literature, fatigue is said to contribute remarkably to missing or existing changes of vergence dynamics for repeated vergence eye movements (Thiagarajan & Ciuffreda, 2013).

Vergence latency showed significant change, decreasing in the first adapted direction but not in the second adapted direction. Again, either transmission or fatigue could account for the differences (Dysli et al., 2015).

Combined saccade–vergence and pursuit–vergence

Although not the focus of this study as tested in these experiments, vergence might have interacted with combined saccades and/or pursuit eye movements. Vergence peak velocity might have been higher when combined with saccades, an effect that was found to be more pronounced in divergence than convergence (Maxwell & King, 1992). These higher dynamics when saccadic and vergence eye movements are combined are also referred to as “saccade–vergence facilitation” (Zee, Fitzgibbon, & Optican, 1992). Contrariwise, saccades are slowed when they are combined with vergence (Collewijn, Erkelens, & Steinman, 1995). However, Hendel and Gur (2012) recently tested two rival schemes to explain combined saccade–vergence eye movements, and their results were incompatible with the intrasaccadic facilitation of the vergence command. According to Collewijn et al. (1995), pure vergence and pure disconjugate version was almost never seen: Divergence more than convergence was associated with saccades, and horizontal saccades always contained a transient divergence–convergence sequence.

Regarding pursuit–vergence interaction, Maxwell and Schor (2004) found that asymmetrical slow eye movements are not controlled monocularly. They contain a vergence component along with symmetrical smooth pursuit.

Conclusion

A horizontal gaze-dependent change of disparity entails a series of rapid modifications in the oculomotor response. Vergence movements become faster, and the level of phoria adapts in two ways. The first is a concomitant adaptation, which affects all directions of gaze. The second is an incommittant adaptation, which is more effective in the gaze direction, which during adaptation required an increased phoria. These adaptive processes promote ocular alignment and thus facilitate binocular vision in all directions of gaze.

Keywords: vergence, phoria, eye movement, plasticity, adaptation, binocular vision

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